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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/730,469	12/04/2000	Anthony P. Heaney	CEDAR-45257	7071

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	17

DATE MAILED: 08/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/730,469	Heaney et al.
Examiner	**Art Unit**
Shin-Lin Chen	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 28, 2003*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-7, 14, 15, 17-23, 42, 43, 46, 47, and 50-57* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-7, 14, 15, 17-21, 23, 42, 43, 46, and 47* is/are rejected.

7) ☒ Claim(s) *22 and 50-57* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' amendment and terminal disclaimer filed 4-28-03 have been entered. Claims 1, 7, 14, 15, 17, 18 and 42 have been amended. Claims 50-57 have been added. Claims 1-7, 14, 15, 17-23, 42, 43, 46, 47 and 50-57 are pending and under consideration.

Claim Objections

1. Claim 1 remains objected and claim 50 is objected to because of the following informalities: The term "and/or" in claims 1 and 50 is improper. Changing the term "and/or" to "...or...or both" would be remedial. Appropriate correction is required. Applicants' amendment filed 4-28-03 necessitates this new ground of rejection for claim 50.

Double Patenting

2. Applicant is advised that should claims 1, 42 and 46 be found allowable, claims 15, 43 and 47, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MEP. § 706.03(k). Applicants' amendment filed 4-28-03 necessitates this new ground of rejection.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-7, 14, 15, 17-21, 23, 42, 43, 46 and 47 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting proliferation of breast carcinoma cells by injecting MCF-7 breast carcinoma cells transfected with expression vector expressing PTTG-C peptide into nude mice, does not reasonably provide enablement for a method of inhibiting neoplastic cellular proliferation or transformation of a mammalian breast or ovarian cell that overexpresses PTTG by delivering any expression vector comprising a polynucleotide encoding a PTTG-C peptide to said cell via administration route other than direct *in situ* administration *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 10-21-02 (Paper No. 13). Applicant's arguments filed 4-28-03 have been fully considered but they are not persuasive.

Applicants cite Exhibit A-C and argue that several gene therapy clinical trials, in which pre-clinical trials have large body of reliable data on animal model, have been underway, a successful model of in utero gene therapy in large mammal, and gene therapy for adenosine deaminase deficiency has some success. Applicants further argue that the specification teaches

how to make expression vector and the use of suitable expression vector for gene therapy, and gene therapy was not unpredictable at the time of the invention (amendment, p. 14, 15). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-21-02 (Paper No. 13). As discussed in the preceding Official action, the art of gene therapy was unpredictable at the time of the invention, one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time". The fate of the DNA vector itself, the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and protein's compartmentalization within the cell, or its secretory fate, once produced are all important factors for a successful gene therapy. In addition, "the choice of vectors and delivery routes depends on the nature of the target cells and the required levels and stability of expression" for gene therapy. Each gene therapy protocol has to be considered case by case because of the difference in the type of disease treated, the vector and the promoter used, the gene expressed, the biological function of the protein expressed, the stability of said protein within cells, and the administration routes used. The success of a gene therapy protocol can not necessarily be extrapolated to success for another gene therapy protocol. Although several gene therapy clinical trials have been underway and some gene therapy protocols might be successful for a particular disease and it was known in the

art to prepare various expression vectors, it does not mean that the *in vivo* gene therapy of the present invention would be enabled because of the unpredictability of gene therapy *in vivo* and various factors that determine the effectiveness of a gene therapy for a particular disease by using a particular gene as discussed above.

Applicants cite Exhibits D-I and argue that it was known in the art to deliver expression vector, such as pseudotyped retroviral vector, to target neoplastic cells and tissues, use of tumor-specific promoter, such as hypoxia-responsive elements, intraarterial delivery of HSV-1 mutant hrR3 vector + gancyclovir to intracerebral 9L tumors in rat, and intratumoral injection of HSV-1 mutant hrR3 in rat. Applicants argue that immunosuppressant cyclophosphamide can reduce the immune response against hrR3 HSV- mutant vector (amendment, p. 15-17). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-21-02 (Paper No. 13) and the reasons set forth above under 35 U.S.C. 112 first paragraph rejection.

Conclusion

5. Claims 1-7, 14, 15, 17-21, 23, 42, 43, 46 and 47 are rejected. Claims 22 and 50 are objected. Claims 51-57 are objected to as being dependent upon a objected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MEP. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

S Chen